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SEARCH REQUEST FORM

Examiner # (Mandatory): _____ Requester's Full Name: PK SRIVASTAVA

Art Unit 1624 Location (Bldg/Room#): CM 1; 4E17 Phone (circle 305 306 308) 4717

Serial Number: 09/508,026 Results Format Preferred (circle): PAPER DISK E-MAIL

Title of Invention EPOXYSUCCINAMIDE DERIVS.

Inventors (please provide full names): NOMURA

Earliest Priority Date: 09/04/1998

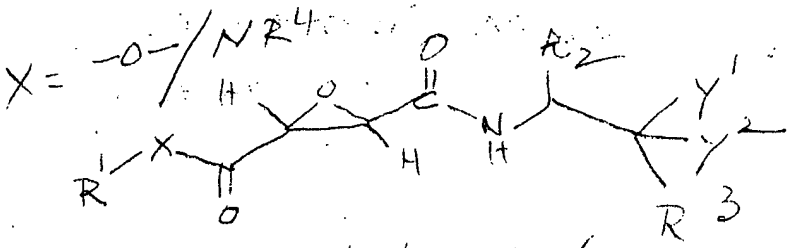
Keywords (include any known synonyms registry numbers, explanation of initialisms):

EPOXY-SUCCINAMIDE DERIVATIVE
METHOD OF TREATING BONE DISEASE
& ARTHRITIS

See claim 1

Search Topic:

Please write detailed statement of the search topic, and the concept of the invention. Describe as specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. You may include a copy of the abstract and the broadcast or most relevant claim(s).



R1 = H/alkyl/aryl/het

R2 = "

John Please Thank

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TECHNICAL INFORMATION SERVICES (STIC)

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Searcher: JOHN DANTZMAN

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Date Picked Up: 7-31-00

Date Completed: 7-31-00

Clerical Prep Time: 20

Terminal Time: _____

Number of Databases: 25

Type of Search

_____ N.A. Sequence
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1 Structure (#)
_____ Bibliographic
_____ Litigation1
_____ Fulltext
_____ Procurement
_____ Other

Vendors (include cost where applicable)

✓ STN
_____ Questel/Orbit
_____ Lexis/Nexis
_____ WWW/Internet
_____ In-house sequence systems (list)
_____ Dialog
_____ Dr. Link
_____ Westlaw
_____ Other (specify)

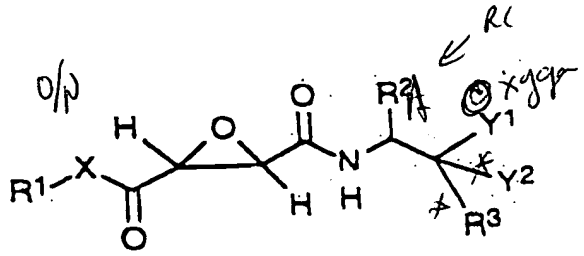
PTO-1590 (2-99)

Submitted 02/08/02

09/508,026

a1

-- 22. An epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt:



(1)

wherein

R^1 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

R^2 represents an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10 carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

R^3 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10

contd.
a 1

carbon atoms, an alkynyl group having 2 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

X represents -O- or -NR^4- in which R^4 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Y^1 represents a hydroxyl group, an alkoxy group having 1 to 6 carbon atoms, an acetoxy group, or an aralkyloxy group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

Y^2 represents a hydrogen atom or an alkyl group having 1 to 10 carbon atoms;

provided that each of the aryl group and the heterocyclic group for R^1 to R^4 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

contd.
a1

23. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 22, wherein R^1 is a hydrogen atom or an alkyl group having 1 to 6 carbon atoms.

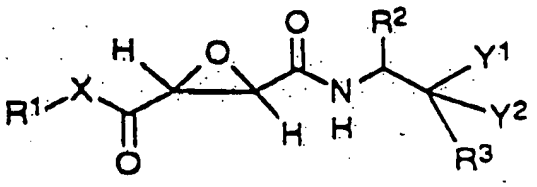
24. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 22, wherein R^2 is an alkyl group having 1 to 6 carbon atoms, phenyl, or benzyl.

25. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 22, wherein R^3 is a hydrogen atom or an aryl group having 6 to 20 carbon atoms.

26. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 22, wherein X is -O-.

27. The physiologically acceptable salt of the epoxysuccinamide derivative defined in claim 22, wherein the physiologically acceptable salt is an alkali metal salt.

28. An epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt:



(1)

wherein

R^1 represents a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an alkenyl group having 2 to 10

contd. a1

2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, and guanidino, and

provided that each of the aryl group and the heterocyclic group for R^1, R^3 and R^5 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

29. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 28, wherein R^1 is a hydrogen atom or an alkyl group having 1 to 6 carbon atoms.

30. The epoxysuccinamide derivative of the formula (1) and its physiologically acceptable salt defined in claim 28, wherein X is -O-.

31. The physiologically acceptable salt of the epoxysuccinamide derivative defined in claim 28, wherein the physiologically acceptable salt is an alkali metal salt.

32. A method for treating bone diseases which comprises injecting or orally administering into a patient an epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt in an amount of 0.01 to 100 mg/day in the case of injection or in an amount of 0.1 mg/day to 1 g/day in the case of oral administration:

contd. a1

alkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

X represents -O- or -NR^4- in which R^4 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms;

Y^1 represents a hydroxyl group, an alkoxy group having 1 to 6 carbon atoms, an acetoxy group, or an aralkyloxy group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

Y^2 represents a hydrogen atom or an alkyl group having 1 to 10 carbon atoms;

provided that each of the aryl group and the heterocyclic group for R^1 to R^4 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

34. A method for treating bone diseases which comprises injecting or orally administering into a patient

contd. a1

atoms;

Y^1 represents OR^5 in which R^5 is a hydrogen atom, an alkyl group having 1 to 10 carbon atoms, an aryl group having 6 to 20 carbon atoms, an aralkyl group comprising an aryl group having 6 to 20 carbon atoms and an alkyl group having 1 to 6 carbon atoms, an acyl group having 2 to 20 carbon atoms, a heterocyclic group having 3 to 12 carbon atoms, or a heterocyclic-alkyl group comprising a heterocyclic group having 3 to 12 carbon atoms and an alkyl group having 1 to 6 carbon atoms; and

Y^2 represents a hydrogen atom;

provided that the alkyl group for R^5 may have one or more substituents selected from the group consisting of hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, and guanidino, and

provided that each of the aryl groups and the heterocyclic groups for R^1, R^3 and R^5 may have one or more substituents selected from the group consisting of alkyl having 1-6 carbon atoms, hydroxyl, amino, alkylamino having 1-6 carbon atoms, dialkylamino having 2-12 carbon atoms in total, alkoxy having 1-6 carbon atoms, halogen, haloalkyl having 1-6 carbon atoms, cyano, nitro, carboxyl, alkoxycarbonyl having 2-7 carbon atoms, carbamoyl, alkylaminocarbonyl having 2-7 carbon atoms, dialkylaminocarbonyl having 3-13 carbon atoms in total, amidino, and guanidino.

35. A method for treating arthritis which comprises injecting or orally administering into a patient an epoxysuccinamide derivative having the following formula (1) and its physiologically acceptable salt in an amount of 0.01 to 100 mg/day in the case of injection or in an

SUMMARY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=> d his

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     FILE 'REGISTRY' ENTERED AT 10:58:45 ON 31 JUL 2000
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L2              50 S L1
L3            1205 S L1 FUL
L4             STR L1
L5              14 S L4 SSS SAM SUB=L3
L6             STR L6
L7              13 S L6 SSS SAM SUB=L3
L8             STR L6
L9              13 S L8 SSS SAM SUB=L3
L10            STR L8
L11              3 S L10 SSS SAM SUB=L3
L12             65 S L10 SSS FUL SUB=L3

     FILE 'CAPLUS' ENTERED AT 11:11:28 ON 31 JUL 2000
L13              8 S L12

     FILE 'CAOLD' ENTERED AT 11:16:03 ON 31 JUL 2000
L14              0 S L12

     FILE 'BEILSTEIN' ENTERED AT 11:16:20 ON 31 JUL 2000
L15              2 S L10 FUL
L16              0 S L12
L17              2 S L15 NOT L16
L18              2 S L15 AND PRE/FA
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65 compounds Reg

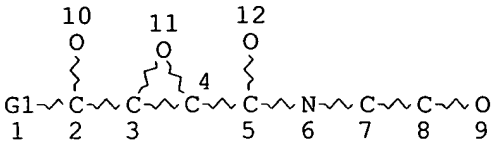
8 cites Caplus

0 cites Caold

2 compounds Beilstein

=> d que l12

L1 STR



Parent Search

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
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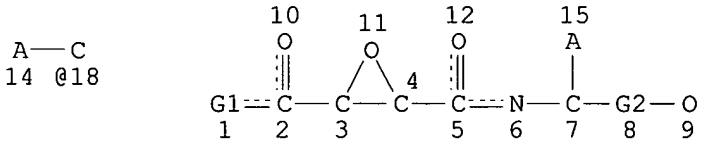
L10 STR



Subset Search to Narrow

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 16

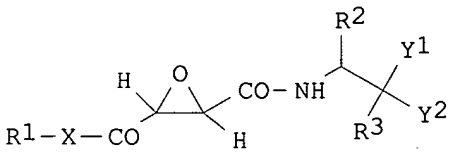
STEREO ATTRIBUTES: NONE
L12 65 SEA FILE=REGISTRY SUB=L3 SSS FUL L10

=> d bib abs hitstr

L13 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2000 ACS
AN 1999:184251 CAPLUS
DN 130:223163
TI Preparation of epoxysuccinamide derivatives for treatment of bone diseases
and arthritis
IN Nomura, Yutaka; Takahashi, Toshihiro; Yoshino, Yasushi; Nishioka, Koichiro
PA Nippon Chemiphar Co., Ltd., Japan
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9911640	A1	19990311	WO 1998-JP3983	19980904
W: AU, CA, CN, JP, KR, RU, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9889978	A1	19990322	AU 1998-89978	19980904
EP 1022276	A1	20000726	EP 1998-941728	19980904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI JP 1997-257538 19970904
WO 1998-JP3983 19980904
OS MARPAT 130:223163
GI



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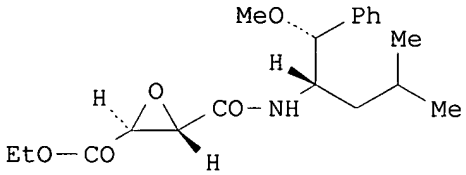

II

applicants

AB Novel epoxysuccinamide derivs. (3-carboxyoxirane-2-carboxamides) represented by general formula (I) or physiol. acceptable salts thereof [wherein R1 and R3 are each H, alkyl, alkenyl, alkynyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; R2 is alkyl, alkenyl, alkynyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; X is O or NR4 (wherein R4 is H, alkyl, aryl, aralkyl, a heterocyclic group, or alkyl substituted with a heterocyclic group); Y1 is OR5, SR6 or NR7R8 (wherein R5, R6 and R7 are each H, alkyl, aryl, aralkyl, acyl, a heterocyclic group, or alkyl substituted with a heterocyclic group; and R8 is the same as defined as to
R4); and Y2 is H or alkyl, or alternatively Y1 and Y2 may be united to

form =O, =S, =N-R9 or =N-OR10 (wherein R9 and R10 are each the same as defined as to R4), with the proviso that the alkyl, aryl and heterocyclic groups defined as to R5 to R10 may each have one or more specific substituents and that the groups defined as to R1 to R10 and Y2 are each specified in the no. of carbon atoms] are prepd. These compds. inhibit bone absorption and activity of cathepsin L and B (cysteine protease) and are useful for the treatment of bone diseases such as osteoporosis, malignant hypercalcemia, and Paget's disease of bone, arthritis deformans and chronic articular rheumatism accompanied by unusual exasperation of cathepsin B and L activity, and muscular dystrophy and muscular atrophy related to cathepsin B and L. Thus, (2S,3S)-3-ethoxycarbonyloxirane-2-carboxylic acid was condensed with (S)-1-[(R)-.alpha.-methoxybenzyl]-3-methylbutylamine using N-hydroxysuccinimide and DCC in EtOAc at room temp.
overnight to give the title compd. (II). II at 15 mg/kg p.o. lowered serum calcium by 20.4% in rat.

IT **221143-71-1P 221143-72-2P 221143-73-3P**
221143-74-4P 221143-75-5P 221143-76-6P
221143-77-7P 221143-80-2P 221143-81-3P
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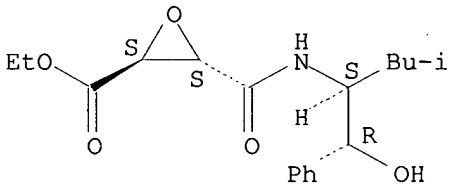
221144-19-0P 221144-20-3P 221144-21-4P
221144-22-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epoxysuccinamide derivs. as bone absorption inhibitors and cathepsin B and L inhibitors for treatment of bone diseases and arthritis)

RN 221143-71-1 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-hydroxyphenylmethyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

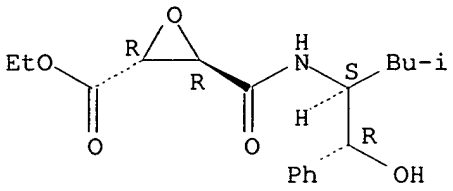
Absolute stereochemistry.



RN 221143-72-2 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-hydroxyphenylmethyl]-3-

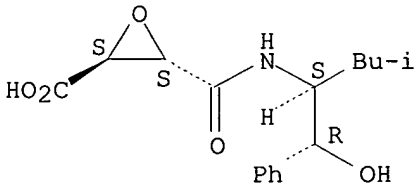
methylbutyl]amino]carbonyl]-, ethyl ester, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



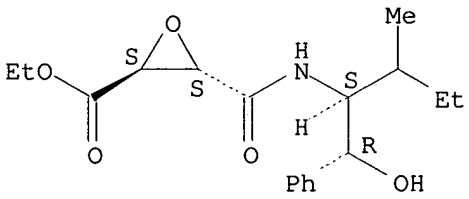
RN 221143-73-3 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-hydroxyphenylmethyl]-3-methylbutyl]amino]carbonyl]-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



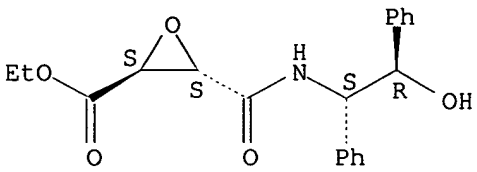
RN 221143-74-4 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-hydroxyphenylmethyl]-2-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



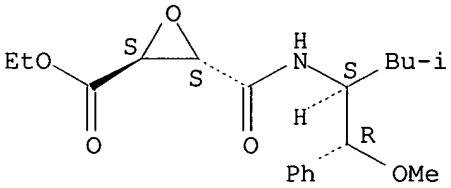
RN 221143-75-5 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S,2R)-2-hydroxy-1,2-diphenylethyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221143-76-6 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-methoxyphenylmethyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221143-77-7 CAPLUS
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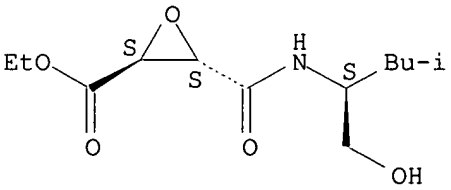
Absolute stereochemistry.



RN 221143-80-2 CAPLUS
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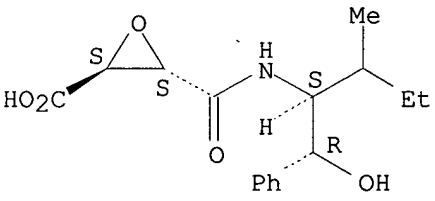
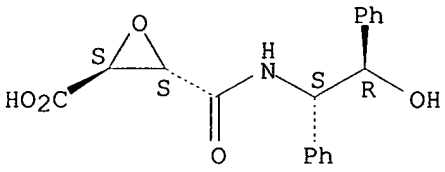
Absolute stereochemistry.



RN 221143-81-3 CAPLUS

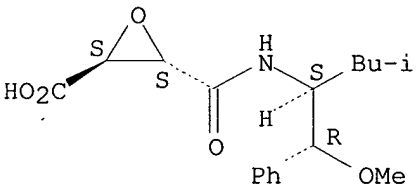
CN Oxiranecarboxylic acid, 3-[[[(1S,2R)-2-hydroxy-1,2-diphenylethyl]amino]carbonyl]-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221143-82-4 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-methoxyphenylmethyl]-3-methylbutyl]amino]carbonyl]-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221143-83-5 CAPLUS
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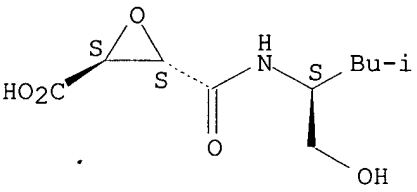
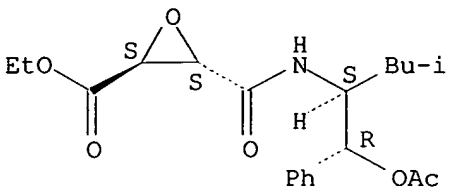
Absolute stereochemistry.



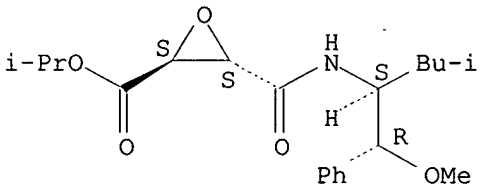
RN 221143-84-6 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-(acetyloxy)phenylmethyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



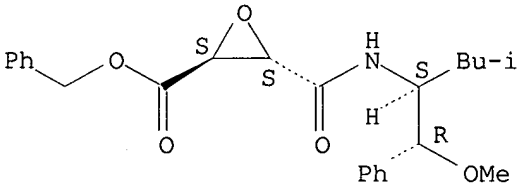
RN 221143-85-7 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-methoxyphenylmethyl]-3-methylbutyl]amino]carbonyl]-, 1-methylethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



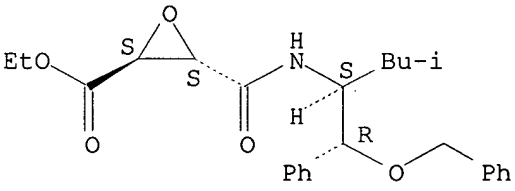
RN 221143-86-8 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-methoxyphenylmethyl]-3-methylbutyl]amino]carbonyl]-, phenylmethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



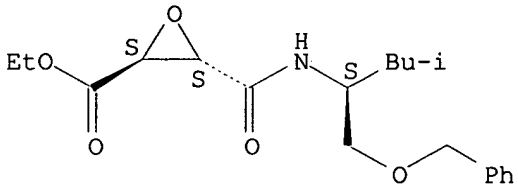
RN 221143-87-9 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(R)-phenyl(phenylmethoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



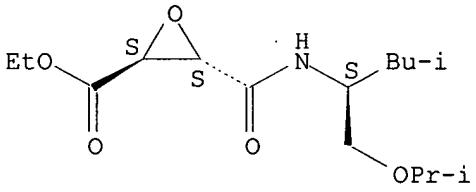
RN 221143-88-0 CAPLUS
CN Oxiranecarboxylic acid,
3-[[[(1S)-3-methyl-1-[(phenylmethoxy)methyl]butyl]
amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



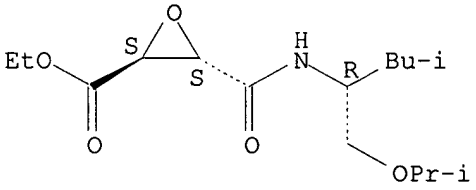
RN 221143-89-1 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(1-
methylethoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



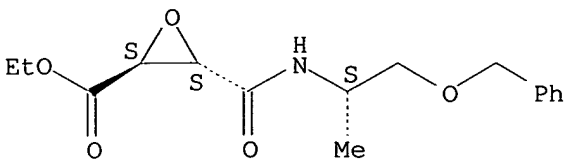
RN 221143-90-4 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1R)-3-methyl-1-[(1-
methylethoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



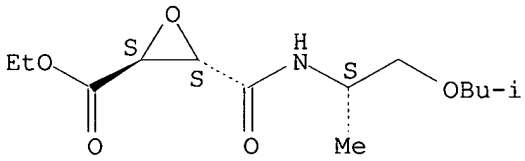
RN 221143-91-5 CAPLUS
CN Oxiranecarboxylic acid,
3-[[[(1S)-1-methyl-2-(phenylmethoxy)ethyl]amino]ca
rbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



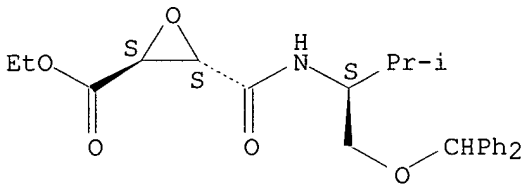
RN 221143-92-6 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-methyl-2-(2-methylpropoxy)ethyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



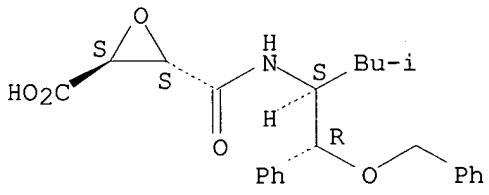
RN 221143-93-7 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(diphenylmethoxy)methyl]-2-methylpropyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221143-94-8 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(R)-phenyl(phenylmethoxy)methyl]butyl]amino]carbonyl]-, (2S,3S)- (9CI) (CA INDEX NAME)

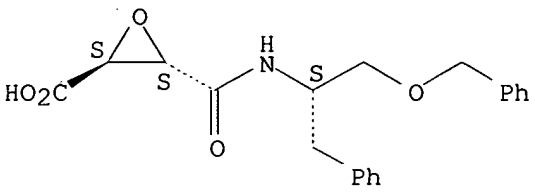
Absolute stereochemistry.



RN 221143-95-9 CAPLUS

CN Oxiranecarboxylic acid, 3-[[[(1S)-2-(phenylmethoxy)-1-(phenylmethyl)ethyl]amino]carbonyl]-, monosodium salt, (2S,3S)- (9CI) (CA INDEX NAME)

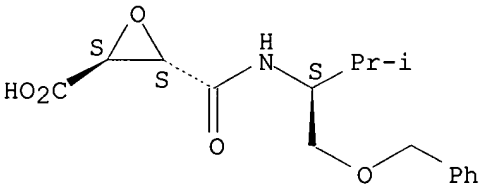
Absolute stereochemistry.



● Na

RN 221143-96-0 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-2-methyl-1-[(phenylmethoxy)methyl]propyl]amino]carbonyl]-, monosodium salt, (2S,3S)- (9CI) (CA INDEX NAME)

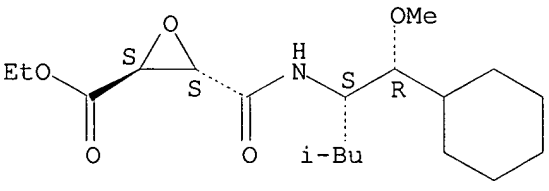
Absolute stereochemistry.



● Na

RN 221143-98-2 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(R)-cyclohexylmethoxymethyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

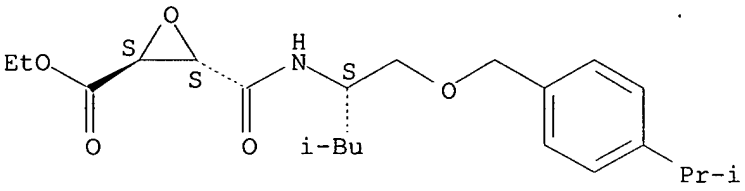
Absolute stereochemistry.



RN 221143-99-3 CAPLUS

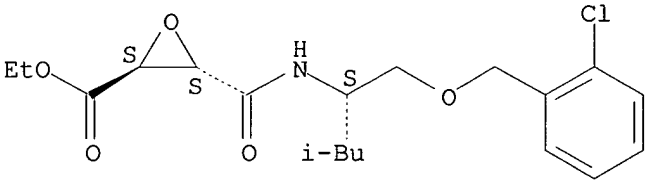
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[[[4-(1-methylethyl)phenyl]methoxy]methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



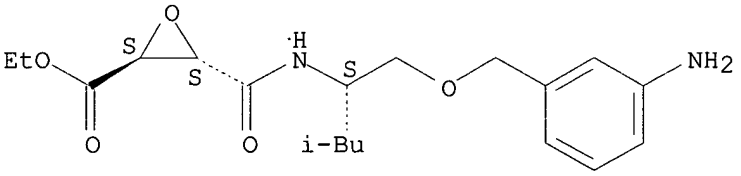
RN 221144-00-9 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[[(2-chlorophenyl)methoxy]methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



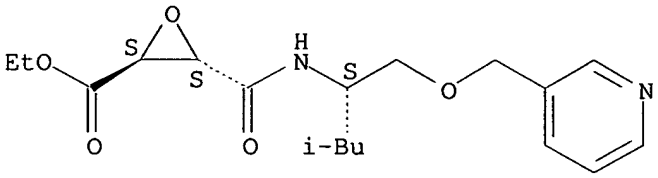
RN 221144-01-0 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[[(3-aminophenyl)methoxy]methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



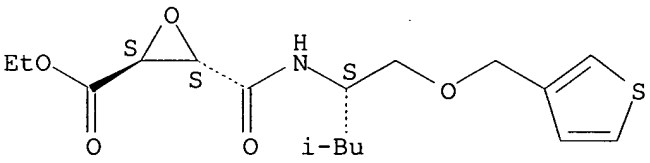
RN 221144-02-1 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(3-pyridinylmethoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



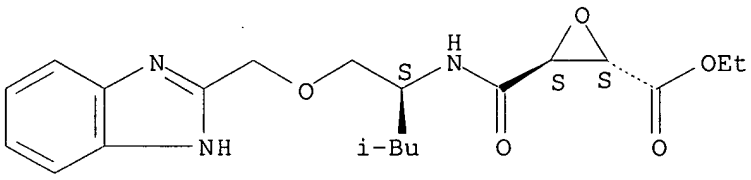
RN 221144-03-2 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(3-thienylmethoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



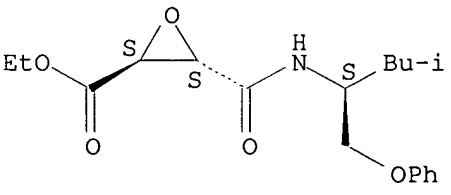
RN 221144-04-3 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(1H-benzimidazol-2-ylmethoxy)methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221144-05-4 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-(phenoxymethyl)butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

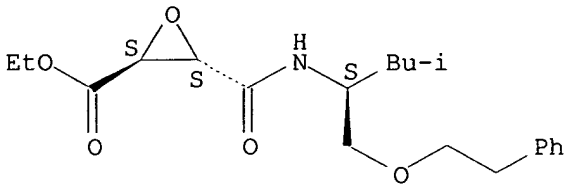
Absolute stereochemistry.



RN 221144-06-5 CAPLUS

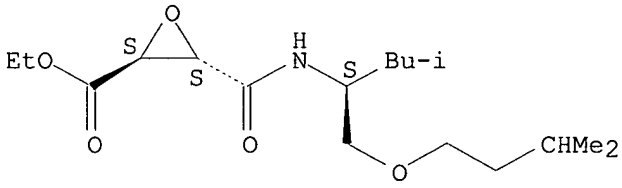
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-phenylethoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



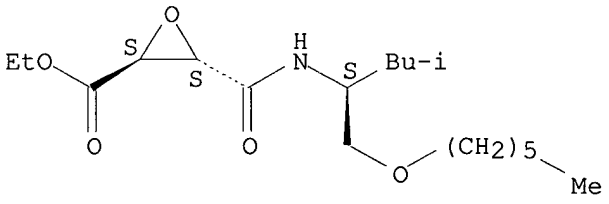
RN 221144-07-6 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(3-methylbutoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



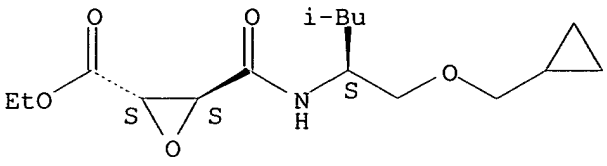
RN 221144-08-7 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(hexyloxy)methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



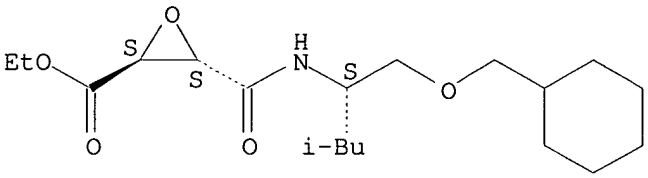
RN 221144-09-8 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(cyclopropylmethoxy)methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



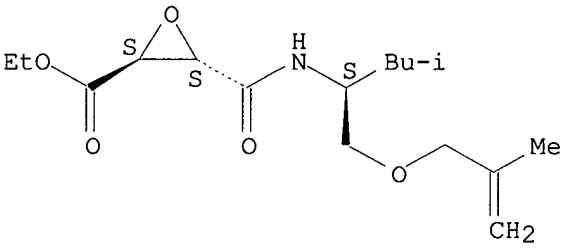
RN 221144-10-1 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(cyclohexylmethoxy)methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



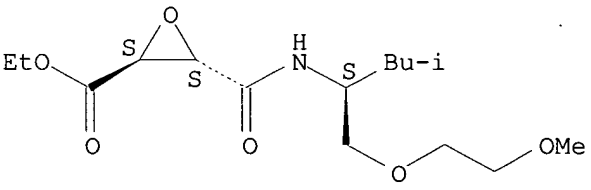
RN 221144-11-2 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[[(2-methyl-2-propenyl)oxy]methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



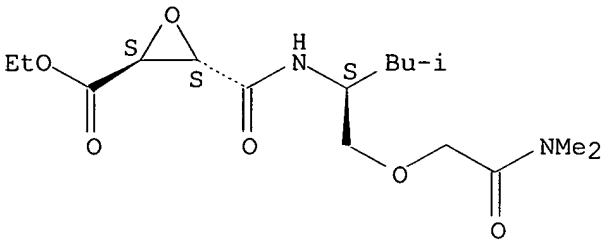
RN 221144-12-3 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[(2-methoxyethoxy)methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



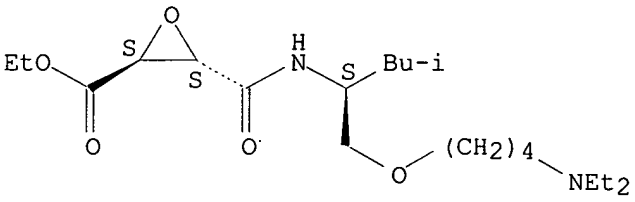
RN 221144-13-4 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[[2-(dimethylamino)-2-oxoethoxy]methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



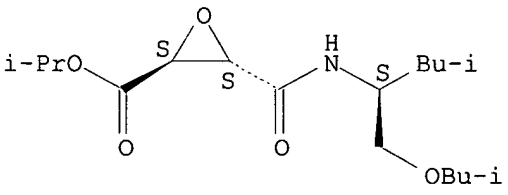
RN 221144-14-5 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-1-[[4-(diethylamino)butoxy]methyl]-3-methylbutyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



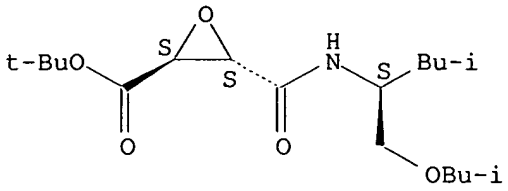
RN 221144-15-6 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, 1-methylethyl ester, (2S,3S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



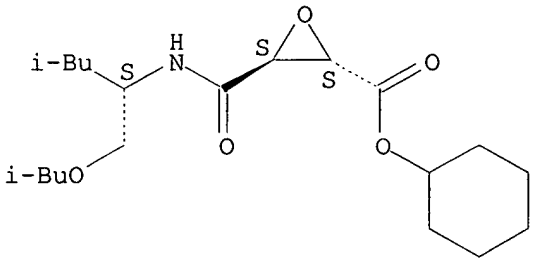
RN 221144-16-7 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



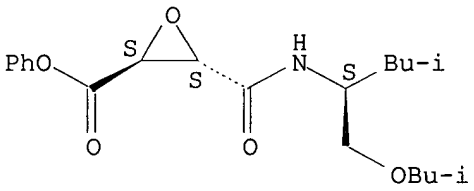
RN 221144-17-8 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, cyclohexyl ester, (2S,3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



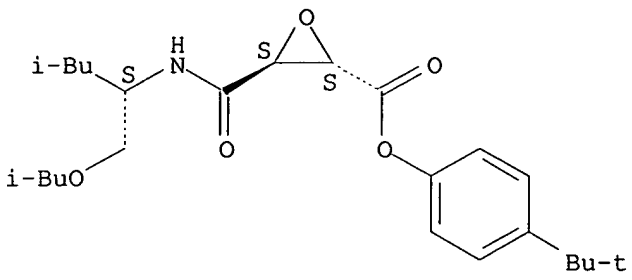
RN 221144-18-9 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, phenyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



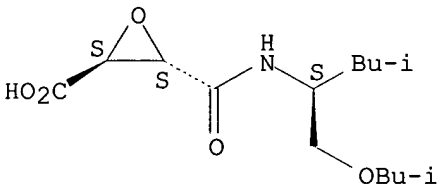
RN 221144-19-0 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, 4-(1,1-dimethylethyl)phenyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221144-20-3 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-3-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, monosodium salt, (2S,3S)- (9CI) (CA INDEX NAME)

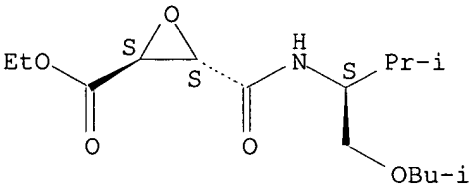
Absolute stereochemistry.



● Na

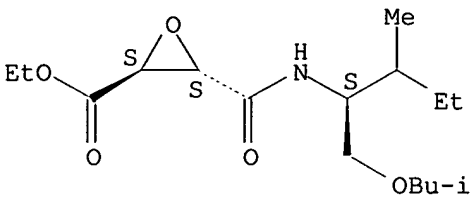
RN 221144-21-4 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-2-methyl-1-[(2-methylpropoxy)methyl]propyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 221144-22-5 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[(1S)-2-methyl-1-[(2-methylpropoxy)methyl]butyl]amino]carbonyl]-, ethyl ester, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



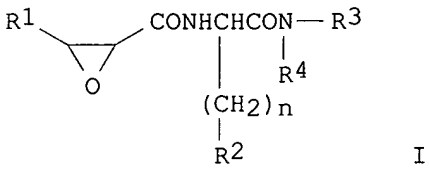
RE.CNT 79
RE
(1) Buttle, D; ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS 1992, V299(2), P377 CAPLUS
(2) Buttle, D; ARTHRITIS & RHEUMATISM 1993, V36(12), P1709 CAPLUS
(3) Feng, M; Protein Engineering 1996, V9(11), P977 CAPLUS
(4) Gour-Salin, B; J Med Chem 1993, V36(6), P720 CAPLUS
(5) Haga, N; Pharmacology 1985, V31(4), P208 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs hitstr 2

L13 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2000 ACS
AN 1995:886024 CAPLUS
DN 123:286713
TI Preparation of epoxysuccinic acid-derivative inhibitors of thiol proteases
for treatment of osteoporosis
IN Tsubotani, Shigetoshi; Takizawa, Masayuki; Shirasaki, Mikio; Fujisawa, Yukio
PA Takeda Chemical Industries, Ltd., Japan
SO Eur. Pat. Appl., 95 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 655447	A1	19950531	EP 1994-307984	19941028
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	US 5556853	A	19960917	US 1994-330833	19941027
	CA 2134627	AA	19950430	CA 1994-2134627	19941028
	FI 9405092	A	19950430	FI 1994-5092	19941028
	NO 9404121	A	19950502	NO 1994-4121	19941028
	AU 9477552	A1	19950518	AU 1994-77552	19941028
	CN 1112555	A	19951129	CN 1994-118687	19941028
	JP 08104683	A2	19960423	JP 1994-265686	19941028
	HU 72319	A2	19960429	HU 1994-3116	19941028
PRAI	JP 1993-272806	19931029			
	JP 1993-272835	19931029			
	JP 1994-186165	19940808			

OS MARPAT 123:286713
GI



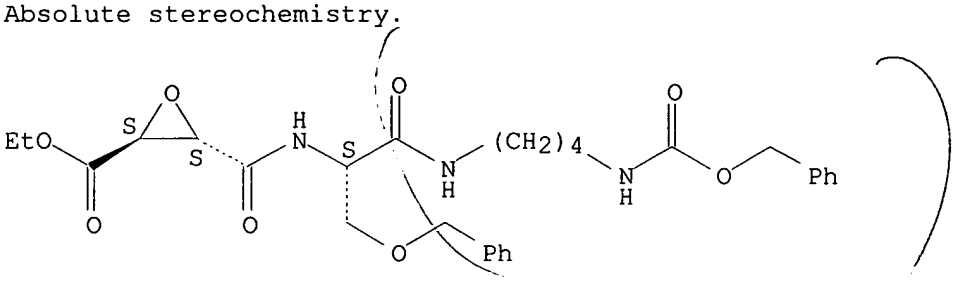
I

AB The title compds. [I; R1 = (un)substituted carboxyl group; R2 = (un)substituted cyclic group; R3 = H, (un)substituted hydrocarbon residue;
R4 = (un)substituted hydrocarbon residue with optionally protected amino group, alkenyl; n = 0-6; R3R4N = heterocyclic residue], which are inhibitors of thiol proteases such as cathepsin L or B, useful as prophylactic and/or therapeutic agents for bone diseases such as osteoporosis, are prepd. and I-contg. formulations presented. Thus, N-Z-N'-[N-(2S,3S)-trans-carboxyoxirane-2-carbonyl]-o-fluoro-L-phenylalanyl]-1,4-diaminobutane (sic) was prepd. and demonstrated a IC50 of 1 ng/mL against cathepsin L and 14 ng/mL against cathepsin B.
IT **169499-72-3P 169499-73-4P 169499-74-5P**

169499-75-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epoxysuccinic acid-deriv. inhibitors of thiol proteases for treatment of osteoporosis)

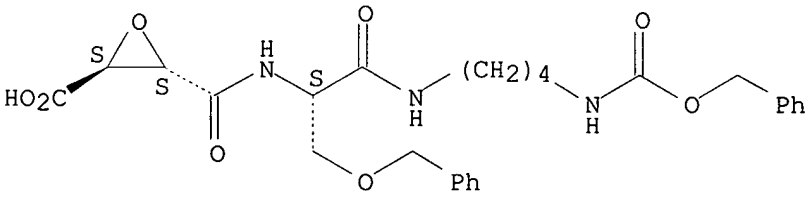
RN 169499-72-3 CAPLUS
CN Oxiranecarboxylic acid, 3-[1,4,11-trioxo-13-phenyl-3-[(phenylmethoxy)methyl]-12-oxa-2,5,10-triazatridec-1-yl]-, ethyl ester, [2S-[2.alpha.,3.beta.(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



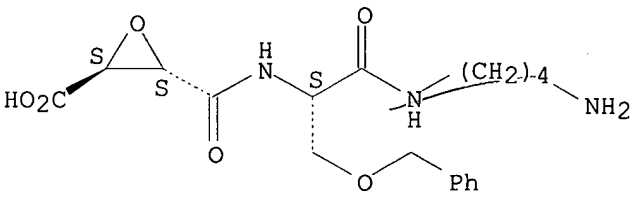
RN 169499-73-4 CAPLUS
CN Oxiranecarboxylic acid, 3-[1,4,11-trioxo-13-phenyl-3-[(phenylmethoxy)methyl]-12-oxa-2,5,10-triazatridec-1-yl]-, [2S-[2.alpha.,3.beta.(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169499-74-5 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[2-[(4-aminobutyl)amino]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]amino]carbonyl]-, [2S-[2.alpha.,3.beta.(R*)]]- (9CI) (CA INDEX NAME)

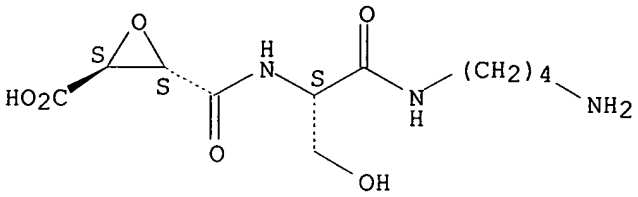
Absolute stereochemistry.



RN 169499-75-6 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[2-[(4-aminobutyl)amino]-1-(hydroxymethyl)-2-

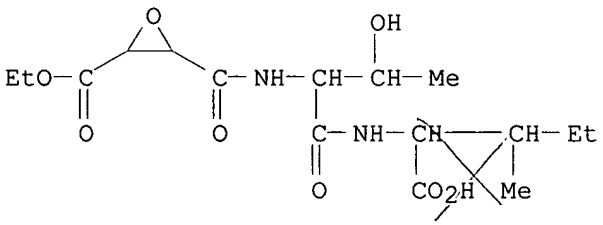
oxoethyl]amino]carbonyl]-, [2S-[2.alpha.,3.beta.(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d bib abs hitstr 3

L13 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2000 ACS
AN 1991:424916 CAPLUS
DN 115:24916
TI Novel epoxysuccinyl peptides. Selective inhibitors of cathepsin B, in vitro
AU Murata, Mitsuo; Miyashita, Satsuki; Yokoo, Chihiro; Tamai, Masaharu; Hanada, Kazunori; Hatayama, Katsuo; Towatari, Takae; Nikawa, Takeshi; Katunuma, Nobuhiko
CS Res. Cent., Taisho Pharm. Co., Saitama, 330, Japan
SO FEBS Lett. (1991), 280(2), 307-10
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
AB A series of new epoxysuccinyl peptides were designed and synthesized to develop a specific inhibitor of cathepsin B. Of these compds., N-(L-3-trans-ethoxycarbonyloxirane-2-carbonyl)-L-isoleucyl-L-proline (compd. CA-030) and N-(L-3-trans-propylcarbamoyloxirane-2-carbonyl)-L-isoleucyl-L-proline (compd. CA-074) were the most potent and specific inhibitors of cathepsin B in vitro. The carboxyl group of proline and the Et ester group or n-propylamide group in the oxirane ring were necessary, the Et ester group or the n-propylamide group being particularly effective for distinguishing cathepsin B from other cysteine proteinases such as cathepsins L and H, and calpains.
IT **134528-17-9**
RL: BIOL (Biological study)
(cathepsin B and other cysteine proteinases inhibition by, specificity of)
RN 134528-17-9 CAPLUS
CN L-Isoleucine, N-[N-[[3-(ethoxycarbonyl)oxiranyl]carbonyl]-L-threonyl]-, (2S-trans)- (9CI) (CA INDEX NAME)

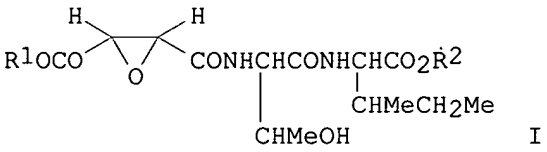


=> d bib abs hitstr 4

L13 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2000 ACS
AN 1991:247800 CAPLUS
DN 114:247800
TI N-(L-trans-3-Carboxyoxirane-2-carbonyl)-L-threonyl-L-isoleucines as thiol protease inhibitors
IN Murata, Mitsuo; Yokoo, Chihiro; Hanada, Kazunori
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

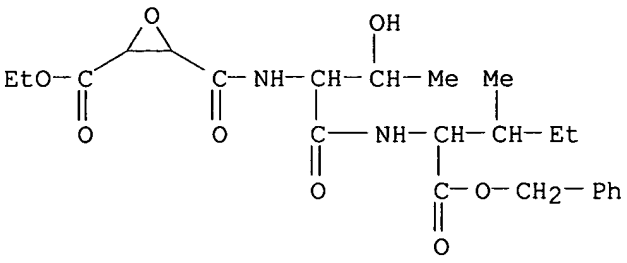
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02304075	A2	19901217	JP 1989-124751	19890518

OS MARPAT 114:247800
GI

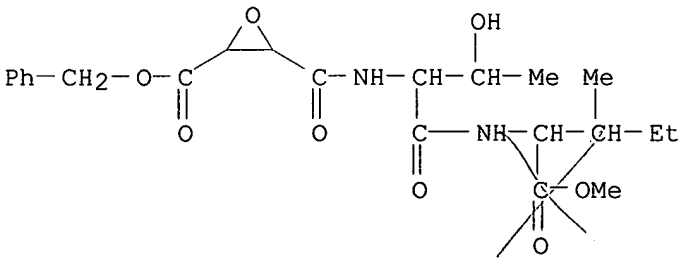


I

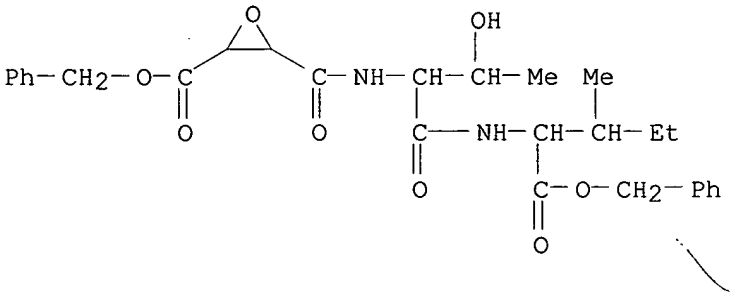
AB The title compds. I (R1, R2 = H., lower alkyl, CH2Ph), useful as inflammation inhibitors (no data) and for treatment of myolytic diseases, e.g. muscular dystrophy related to CANP (Ca-dependent neutral protease) and cathepsin B, are prepd. An AcOEt soln. of 1.15 g L-trans-epoxysuccinic acid Et p-nirtophenyl ester was added dropwise to an AcOH soln. of 1.20 g L-threonyl-L-isoleucine benzyl ester at 0.degree. and the reaction mixt. was further stirred at 0.degree. for 1 h then at room temp. overnight to give 1.21 g I (R1 = Et, R2 = CH2Ph), 500 mg of which in EtOH contg. Pd/C was stirred under H at room temp. for 1 h to give 314 mg I (R1 = Et, R2 = H) (II). IC50 value of II against cathepsin B was 410 nM, vs. >200,000 nM against CANP and >100,000 against papain.
IT **133824-71-2P 133824-72-3P 133824-73-4P**
133824-74-5P 133824-75-6P 133824-76-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as cathepsin B inhibitor)
RN 133824-71-2 CAPLUS
CN L-Isoleucine, N-[N-[[3-(ethoxycarbonyl)oxiranyl]carbonyl]-L-threonyl]-, phenylmethyl ester, (2R-trans)- (9CI) (CA INDEX NAME)



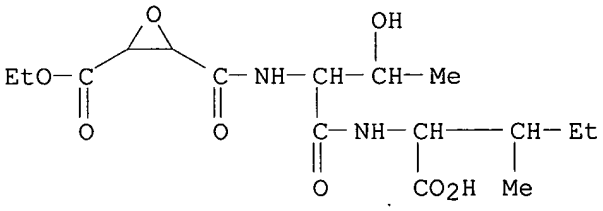
RN 133824-72-3 CAPLUS
CN L-Isoleucine, N-[N-[[3-[(phenylmethoxy)carbonyl]oxiranyl]carbonyl]-L-threonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)



RN 133824-73-4 CAPLUS
CN L-Isoleucine, N-[N-[[3-[(phenylmethoxy)carbonyl]oxiranyl]carbonyl]-L-threonyl]-, phenylmethyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

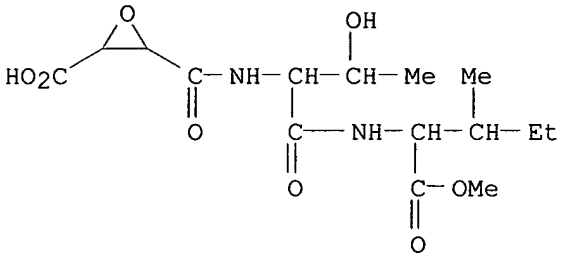


RN 133824-74-5 CAPLUS
CN L-Isoleucine, N-[N-[[3-(ethoxycarbonyl)oxiranyl]carbonyl]-L-threonyl]-, (2R-trans)- (9CI) (CA INDEX NAME)

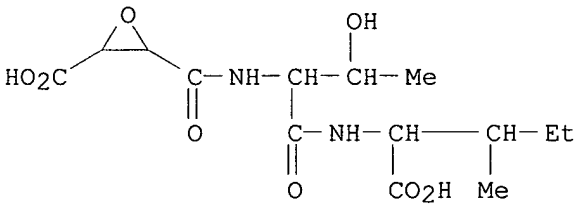


Searched by John Dantzman 308-4488

RN 133824-75-6 CAPLUS
CN L-Isoleucine, N-[N-[(3-carboxyoxiranyl)carbonyl]-L-threonyl]-, 1-methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

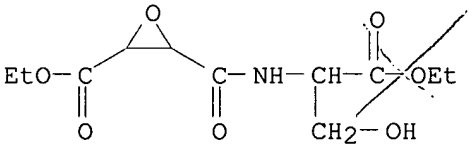


RN 133824-76-7 CAPLUS
CN L-Isoleucine, N-[N-[(3-carboxyoxiranyl)carbonyl]-L-threonyl]-, (2R-trans)-
(9CI) (CA INDEX NAME)

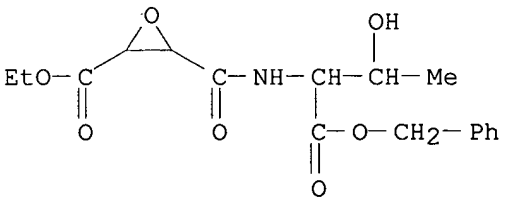


=> d bib abs hitstr 5

L13 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2000 ACS
AN 1981:402502 CAPLUS
DN 95:2502
TI Study on thiol protease inhibitors. Part IV. Relationship between structure and papain inhibitory activity of epoxysuccinyl amino acid derivatives
AU Tamai, Masaharu; Adachi, Takashi; Oguma, Kiyoshi; Morimoto, Shigeo; Hanada, Kazunori; Ohmura, Sadafumi; Ohzeki, Masahiro
CS Res. Lab., Taisho Pharm. Co., Ltd., Saitama, 330, Japan
SO Agric. Biol. Chem. (1981), 45(3), 675-9
CODEN: ABCHA6; ISSN: 0002-1369
DT Journal
LA English
AB A no. of amino acid derivs. of DL-trans-epoxysuccinic acid, with a general formula of R1O-ES-AA-OR2 (ES, DL-trans-epoxysuccinyl group; AA, amino acid residue) were synthesized and used for the study of structure-activity relations of papain inhibition. Branched-alkyl amino acids, such as leucine, valine, and isoleucine, as AA and H or an alkyl group substituted with a Ph or cycloalkyl group as R1 were desirable for activity, resp. However, R2 or the optical activities of ES and AA had less influence on the activity.
IT **68363-00-8 75582-71-7**
RL: BIOL (Biological study)
(papain inhibition by, mol. structure in relation to)
RN 68363-00-8 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[1-(ethoxycarbonyl)-2-hydroxyethyl]amino]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



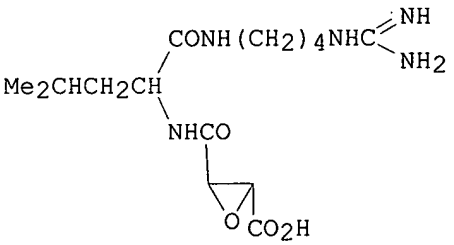
RN 75582-71-7 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[2-hydroxy-1-[(phenylmethoxy)carbonyl]propyl]amino]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



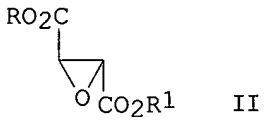
Searched by John Dantzman 308-4488

=> d bib abs hitstr 6

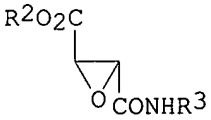
L13 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2000 ACS
AN 1980:639854 CAPLUS
DN 93:239854
TI A specific thiolprotease inhibitor, E-64 and its derivatives
AU Hanada, Kazunori; Tamai, Masaharu; Morimoto, Shigeo; Adachi, Takashi; Oguma, Kiyoshi; Ohmura, Sadafumi; Ohzeki, Masahiro
CS Res. Lab., Taisho Pharm. Co., Ltd., Saitama, 1-403, Japan
SO Pept. Chem. (1980), Volume Date 1979, 17th, 31-6
CODEN: PECHDP
DT Journal
LA English
GI



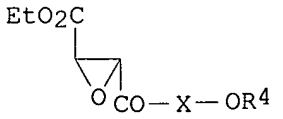
I



II



III

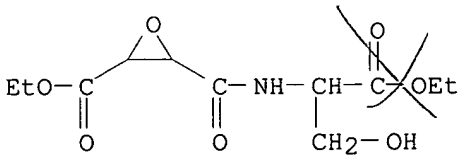


IV

AB E-64 proteinase inhibitor (I), oxiranedicarboxylates II (R, R1 = aralkyl, cycloalkyl, K), oxiranecarboxamides III (R2 = alkyl, aralkyl; R3 = aryl, aralkyl), and oxiranylcarbonyl amino acids IV (R4 = PhCH2, Me, Et; X = amino acid residue, e.g., Ala, Ser, Tyr) were prepd. Papain inhibitory activities were detd. for II-IV and their mol. structure-activity relationships were discussed.

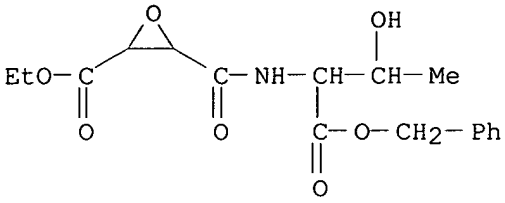
IT **68363-00-8P 75582-71-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and papain inhibiting activity of)

RN 68363-00-8 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[1-(ethoxycarbonyl)-2-hydroxyethyl]amino]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



Searched by John Dantzman 308-4488

RN 75582-71-7 CAPLUS
CN Oxiranecarboxylic acid,
3-[[[2-hydroxy-1-[(phenylmethoxy)carbonyl]propyl]a
mino]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

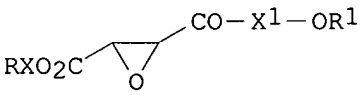


=> d bib abs hitstr 7

L13 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2000 ACS
AN 1980:586790 CAPLUS
DN 93:186790
TI Epoxysuccinyl amino acids
IN Sawada, Jiro; Hanada, Kazunori; Tamai, Masaharu; Morimoto, Shigeo; Omura, Sadafumi
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

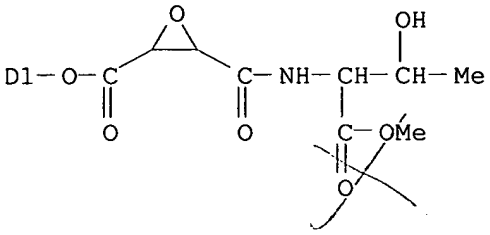
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 55035012	A2	19800311	JP 1978-107766	19780902
JP 61055508	B4	19861128		

GI

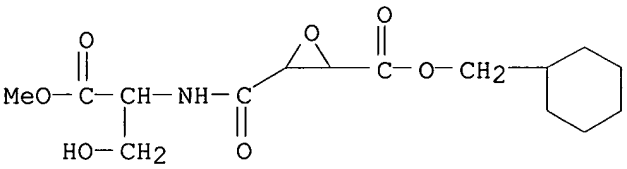


I

AB The title compds. I [X = alkylene, X1 = amino acid residue, R = (un)substituted cycloalkyl, cycloalkenyl, R1 = alkyl, CH2Ph, (cycloalkyl)alkyl] were prepd. from the appropriate succinyl chlorides and amino acid esters. Thus, epoxysuccinic acid mono(cyclopentylpropyl) ester chloride, obtained from 1.4 g epoxysuccinic acid mono(cyclopentylpropyl) ester K salt and (COCl)2, was treated with L-leucine Et ester in Et2O contg. Et3N for 3 h to give 1.28 g N-[3-[(3-DL-cyclopentylpropyl)oxycarbonyl]-2-oxiranylcarbonyl]-L-leucine Et ester.
IT **75148-92-4P 75186-12-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 75148-92-4 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[2-hydroxy-1-(methoxycarbonyl)propyl]amino]carbonyl]-, bicyclo[2.2.2]octyl ester (9CI) (CA INDEX NAME)



RN 75186-12-8 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[1-(hydroxymethyl)-2-methoxy-2-oxoethyl]amino]carbonyl]-, cyclohexylmethyl ester (9CI) (CA INDEX NAME)

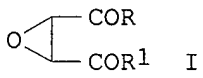


=> d bib abs hitstr 8

L13 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2000 ACS
AN 1979:87233 CAPLUS
DN 90:87233
TI Epoxysuccinic acid derivatives
IN Sawada, Jiro; Hanada, Kazunori; Tamai, Masaharu; Morimoto, Shigeo; Omura, Sadafumi
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Ger. Offen., 56 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2809036	A1	19780907	DE 1978-2809036	19780302
	DE 2809036	C2	19870108		
	JP 53108923	A2	19780922	JP 1977-23092	19770303
	JP 60059232	B4	19851224		
	JP 53108936	A2	19780922	JP 1977-23536	19770304
	JP 60037104	B4	19850824		
	JP 53108948	A2	19780922	JP 1977-23537	19770304
	JP 60037105	B4	19850824		
	GB 1595168	A	19810812	GB 1978-4717	19780206
	FR 2382447	A1	19780929	FR 1978-4933	19780221
	FR 2382447	B1	19810731		
	US 4393228	A	19830712	US 1978-880180	19780222
	BE 864505	A1	19780904	BE 1978-185628	19780302
	CH 629492	A	19820430	CH 1978-2297	19780303
PRAI	JP 1977-23092	19770303			
	JP 1977-23536	19770304			
	JP 1977-23537	19770304			

GI

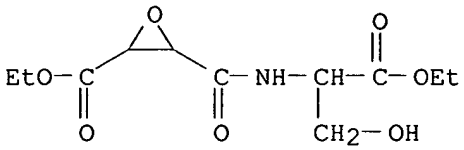


I

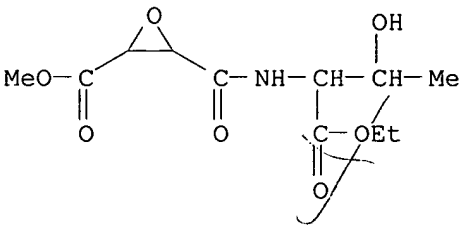
AB Epoxysuccinic acid derivs. I (R = substituted alkoxy, cycloalkoxy; R1 = R, OH, OK, amino acid residue) (220 compds.) were prepd. Thus I (R = R1 = Cl) was treated with cyclohexanol to give 75% I (R = R1 = cyclohexyloxy) which had a papain inhibiting ED50 of 1.98 .mu.g/mL and at 100 mg/kg orally in rats caused 82.1% inhibition of adjuvant arthritis.

IT **68363-00-8 68363-04-2**
RL: RCT (Reactant)
(protease inhibiting activity of)

RN 68363-00-8 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[1-(ethoxycarbonyl)-2-hydroxyethyl]amino]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

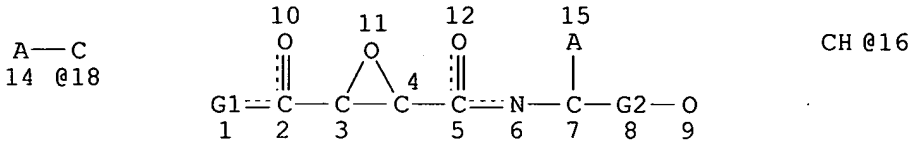


RN 68363-04-2 CAPLUS
CN Oxiranecarboxylic acid, 3-[[[1-(ethoxycarbonyl)-2-hydroxypropyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



=> d que l15

L10 STR



VAR G1=O/N
VAR G2=16/18
NODE ATTRIBUTES:
NSPEC IS RC AT 14
NSPEC IS RC AT 15
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L15 2 SEA FILE=BEILSTEIN SSS FUL L10

=> d

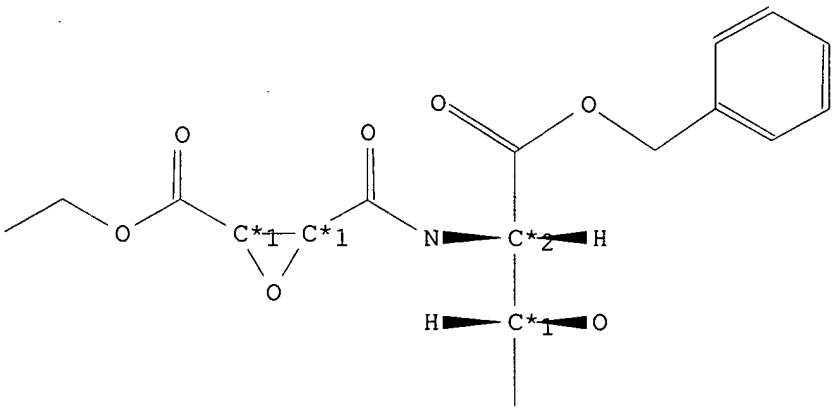
L18 ANSWER 1 OF 2 BEILSTEIN COPYRIGHT 2000 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 7102798 Beilstein
Molecular Formula (MF): C17 H21 N O7
Autonom Name (AUN): 3-(1-benzyloxycarbonyl-2-hydroxy-propylcarbamoyl)-oxirane-2-carboxylic acid ethyl ester
Beilstein Reference (SO): 6-18
General Comments (NTE): Stereo compound; racemate
Formula Weight (FW): 351.36
Lawson Number (LN): 19617; 5228; 3559; 298

Ring System Data:

Number of Rings (CNR): 2
Ring Systems (CNRS): 2
Diff. Ring Systems (CNDRS): 2
Ring Heteros (CNRH): 1
Acyclic Heteros (CNAH): 7

Beilstein Ring Index (BRIX)	Ring System Formula (RF)	BRIX Count
3.1.0-1.2-0.0	C2O	1
6.1.0-0.0-3.1	C6	1



Atom/Bond Notes:
1. CIP Descriptor: R
2. CIP Descriptor: S
Fragment Notes:
Additionally represents mirror image

Preparation:

Searched by John Dantzman 308-4488

PRE

Start: BRN=7090530 C6H7ClO4, BRN=3545845 (2S,3R)-threonine benzyl ester
Reag: Et3N
Time: 3 hour(s)
Solv: diethyl ether
Ambient Temperature
Reference(s):
1. Tamai, Masaharu; Adachi, Takashi; Oguma, Kiyoshi; Morimoto, Shigeo; Hanada, Kazunori; et al., Agric.Biol.Chem., 45 <1981> 3, 675-680, LA: EN, CODEN: ABCHA6

=> d 2

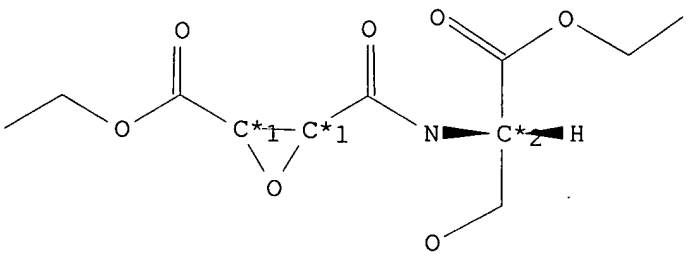
L18 ANSWER 2 OF 2 BEILSTEIN COPYRIGHT 2000 BEILSTEIN CD&S

Beilstein Reg. No. (BRN): 7099267 Beilstein
Molecular Formula (MF): C11 H17 N O7
Autonom Name (AUN): 3-(1-ethoxycarbonyl-2-hydroxy-ethylcarbamoyl)-oxirane-2-carboxylic acid ethyl ester
Beilstein Reference (SO): 6-18
General Comments (NTE): Stereo compound; racemate
Formula Weight (FW): 275.26
Lawson Number (LN): 19617; 3549; 298

Ring System Data:

Number of Rings (CNR): 1
Ring Systems (CNRS): 1
Diff. Ring Systems (CNDRS): 1
Ring Heteros (CNRH): 1
Acyclic Heteros (CNAH): 7

Beilstein Ring Index (BRIX)	Ring System Formula (RF)	BRIX Count
3.1.0-1.2-0.0	C2O	1



Atom/Bond Notes:
1. CIP Descriptor: R
2. CIP Descriptor: S
Fragment Notes:
Additionally represents mirror image

Preparation:
PRE
Start: BRN=7090530 C6H7ClO4, BRN=1721946 L-serine ethyl ester
Reag: Et3N
Time: 3 hour(s)
Solv: diethyl ether
Ambient Temperature
Reference(s):

Searched by John Dantzman 308-4488